

Transcript Details

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Advancements in mRNA Therapeutics for Autoimmune Diseases

Announcer:

Welcome to *Innovations in Medicine*, sponsored by Moderna. This is a non-certified educational series produced and controlled by ReachMD and is intended for healthcare professionals only. On this episode, we'll hear from Dr. Hyunjoon Kim about the mRNA therapeutics that are currently in development for autoimmune diseases. Dr. Kim is an Assistant Professor in the department of pharmaceutical chemistry at the University of Kansas. Let's hear from him now.

Dr. Kim:

So the mRNA 6231 product is actually RNA therapeutics, which deliver the RNA that encodes the IL-2 which is a cytokine that can have immuno modulatory effect in the body.

So, IL-2 can do two things. First of all, it usually proliferates and activates the effector T cells and NK cells to attack the foreign pathogens. However, IL-2, when it's given by a low dose and chronically, what it can do is to actually rather than activating the T cells, it can actually activate the regulatory T cells, which actually suppresses the activation of the T cells and NK cells. So that's why the delivery of the RNA that encodes IL-2 can be used for the autoreactive autoimmune diseases.

So, these R-IL-2 RNA are selective to the IL-2 receptor on the regulatory T cells. So when it's delivered to the subcutaneous injection, the cells can produce the IL-2, which can be taken up by the regulatory T cells, and then the regulatory T cells will proliferate and expand and activated in order to be effective to neutralize the auto reactive T cells and NK cells that attack our own body system. This product is now in clinical trial for the validation of the safety and tolerability, and then tested for the other applications as well.

So, the 6981 is little different from the 6231. So, 6231 is actually we want to produce the IL-2 cytokine in our body. However, the 6981, what it does is that it actually want the body's immune cells to express the molecule named PDL-1. So PDL-1 is a ligand of the PD-1. So, PD-1 is expressed on the effector T cells and NK cells. However, if the PD-1 is triggered by its ligand, the PDL-1, these cells are no longer functional, which means that the expression of the PDL-1 on the immune cells can actually switch off the effector cells. So that's why it can be used for the autoimmune disease, because we can actually switch off the autoreactive T cells and NK cells by promoting the expression of the PDL-1 on the surface of the myeloid cells by delivery of the mRNA 6981. So, that's why the mechanism is different from the 6231.

I think the RNA therapeutics will make a huge impact in the field of autoimmune disease. So current medications for the autoimmune disease therapy includes steroids, and like rapamycin. So, these RNA therapeutics are very novel in the field. So one of the reasons is that once we have a good formulation to deliver the RNA for the human patient, we can simply modify the RNA in order to selectively deliver the pathogens or proteins in the body that can play a different role in the body and autoimmune disease is one of them. So, the benefit of the RNA therapeutics in the autoimmune disease is that its flexibility and the versatility treat the target disease.

So, however, there are some challenges in the RNA therapeutics, which will be to induce the antigen-specific responses and also focused on the localized therapy and also the formulations that can induce the long-term therapy in the autoimmune diseases. So, I think some of the challenges that are related to the modification of RNA and the formulation itself. But other than that, once this formulation, these are met, I think a lot of autoimmune disease therapeutics can be developed based on the RNA therapeutics.

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